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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/704,272	11/01/2000	Alan D. Attie	960296.96668	1921

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/704,272	ATTIE ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,11,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23* is/are allowed.

6)☒ Claim(s) *1,6 and 11* is/are rejected.

7)☒ Claim(s) *2 and 22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment filed 16 November 2005 has been entered. Claim 1 has been amended. Claim 23 has been added and reads on the elected invention. Claims 3-5, 7-10 and 12-21 have been cancelled. Claims 1, 2, 6, 11, 22 and 23 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

35 *USC § 112, second paragraph - indefinite claim language*

The rejection of Claim 5 for reciting "direct drug inhibition" is *withdrawn*. Applicants cancelled Claim 5 (16 November 2005).

Maintained/New Objections and/or Rejections

Claim Objections-

Claims 2, and 22 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections- 35 USC § 112, first paragraph - lack of enablement

Claims 1, 6 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for the limitations of the claims wherein cholesterol uptake in the gut is inhibited by administering an antibody, orally.

Claims 1, 6 and 11 read on a method of inhibiting cholesterol uptake in the gut of a human or animal, by administering an oral antibody as an inhibitor of ABC1.

The specification discloses the *WHAM* mutation in chickens, in which a single nucleotide substitution results in an amino acid change at residue 89 of a chicken ABC transporter. The specification documents the phenotypes of WHAM chickens as to pigmentation, phospholipid disposition and cholesterol transport (Specification pp. 25-27). *WHAM* chickens appear to share similarities to humans with Tangier's disease, such as retention of cholesterol esters in skin and connective tissues (Lawn, et al, 1999, J. Clinical Investigation, 104: 25-31). WHAM chickens and humans with Tangier's disease have reduced abilities for "reverse" cholesterol transport; this means that the pathways leading to excretion of excess cholesterol are severely compromised. In addition, concentrations of high-density cholesterol carrier proteins ("HDL" in humans) in homozygous recessive individuals are 1-5% of the normal or wild-type. These defects in cholesterol processing result in severe neuropathies, premature atherosclerosis, and early death (Remaley, et al, 1999, Proc. Natl. Acad. Sci., 96(22): 12685-12690; Asztalos, et al, 2001, Atherosclerosis, 156: 217-225).

Applicants argue that they specifically teach and envision monoclonal antibodies which are specific for the extracellular domains of the ABC1 protein, and that these domains are recited on pages 6 and 7 of the Specification (page 4, 16 November 2005).

Applicant's arguments filed 16 November 2005 have been fully considered but are not deemed persuasive for the following reasons:

The claims read on a method of inhibiting cholesterol uptake in the gut using antibodies as ABC inhibitors. However, there is no enabling discussion or working examples disclosed in the instant application as to how to practice the method of inhibiting cholesterol uptake in the gut of an animal or human by orally administering oral antibodies. Orally-delivered ABC1 antibodies, besides not being confirmed as functional antagonists of the transporter, would most likely be digested, probably before they had ever reached their target. Claimed methods, particularly treatment methods, must be worked out more-or-less completely at the time of filing of a patent application. Claiming routes of administration that have been shown to be largely ineffective with proteins, and then not describing sufficient details- such as doses, solvents, carriers, etc- indicates that significant experimentation must be undertaken to enable these methods. As suggested previously, routes of administration can have a dramatic effect on drug disposition, and on peptide disposition in particular (Pettit and Gombotz, 1998, TIBTECH, 16: 343-349, Table 1, for example). As suggested above, antibodies are almost certainly *digested* when administered orally. Likewise, proteases abound in many tissues. These examples and others illustrate that the route of administration disclosed in the instant Specification does not reasonably predict untested routes of administration.

Proper analysis of the Wands factors was provided in the previous Office Action (17 May 2005). Due to the large quantity of experimentation required to: determine how to administer, control side effects, and use an antibody orally to inhibit net cholesterol transport across the gut, the lack of direction or guidance in the specification regarding the same, the lack of working examples that use a sulfonylurea *in-vivo*, the state of the art showing the complexities of cholesterol transport regulation, and the breadth of the claims which embrace in-vivo inhibition of net cholesterol transport using oral antibodies--undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Written Description

Claims 1, 6 and 11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1, 6 and 11 read on a method of inhibiting cholesterol transport across the lumen of the gut of a human or animal, by administering an oral antibody as an inhibitor of ABC1.

The Specification teaches use of sulfonylureas to inhibit ABC1 transport. The instant Specification also discusses the critical involvement of the ABC transporter in the WHAM chicken and in Tangier's disease in humans. However, the specification does not teach use of antibodies orally to inhibit the ABC transporter in the gut. The use of sulfonylureas is not adequate written description of use of an entire genus of functionally equivalent ABC1 inhibitors.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the single genus of compounds referred to above, the skilled artisan cannot envision oral use of any other ABC1 inhibitor, including antibodies or other peptides. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the methods disclosed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of using it. Use of the compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only use of sulfonylureas, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

Claims 1, 6 and 11 are rejected. Claims 2 and 22 are objected to. Claim 23 is allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
4 February 2006

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